Physiology-Based Diagnosis Algorithm for Arteriovenous Fistula Stenosis Detection

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Abstract— **In this paper, a diagnosis algorithm for arteriovenous fistula (AVF) stenosis is developed based on auscultatory features, signal processing, and machine learning. The AVF sound signals are recorded by electronic stethoscopes at pre-defined positions before and after percutaneous transluminal angioplasty (PTA) treatment. Several new signal features of stenosis are identified and quantified, and the physiological explanations for these features are provided. Utilizing support vector machine method, an average of 90% two-fold cross-validation hit-rate can be obtained, with angiography as the gold standard. This offers a non-invasive easy-to-use diagnostic method for medical staff or even patients themselves for early detection of AVF stenosis.**

I. Introduction

End-stage renal disease (ESRD) is widespread around the world in recent years. [1] For those suffering from ESRD, hemodialysis is the most common treatment. Blood is withdrawn from the patient's body, purified by a hemodialysis machine, and then returned to the patient's vein. As the blood volume for hemodialysis treatment is typically too large for vein to handle, surgeons usually create an arteriovenous fistula (AVF) as a vascular access which connecting an artery and a vein. The pressure difference between the artery and the vein would enlarge the vein, which made it a suitable vascular access for hemodialysis treatment.

Since AVF is not a natural passageway for blood circulation, the friction between the blood and the vessel wall would cause abnormal narrowing of the vessel, which is called venous stenosis. Venous stenosis is the most common AVF complication, which may cause thrombosis and eventually induce myocardial infarction or cerebrovascular embolism. An early stage AVF stenosis can be released by percutaneous transluminal angioplasty (PTA), but a complicated surgery is required if the stenosis becomes severe. Therefore, the early detection of AVF stenosis appears to be an important issue.

Typical methods for AVF stenosis diagnosis include angiography, color-duplex ultrasound, and physical examination. Angiography is considered the golden rule for AVF stenosis diagnosis, but this method is not only invasive, expensive, but also has serious side effects. Color-duplex ultrasound is a non-invasive method, but it needs to be performed in hospitals. Physical examination can be performed by a skilled operator by auscultation and palpation [2]. When stenosis occurs, the turbulence flow creates audible sound which can be identified by the physician. However, a skilled operator is still required for such evaluation.

Previous works have discussed several AVF stenosis diagnosis algorithms based on acoustical detection [3]-[10]. Typically, electronic stethoscopes are used for data acquisition. Then the sound data is analyzed and classified. The feature extraction algorithm plays the most important role in such system. Previous research based on various signal characteristics, such as the energy of high band signal [3]-[6], the energy distribution of the signal, the envelope of the time-domain waveform [8]-[9], the S-transform of segmented signal [10], etc. Besides, most of the data sets in previous works are not large enough to develop a diagnosis system for stenosis occurring in different positions, different levels of severity, and different patients. Due to the complexity and variance of stenosis morphology, several major difficulties remained to be solved. The following are three primary difficulties when developing a feature extraction algorithm for AVF stenosis diagnosis.

1) Stenosis may have different levels of severity, and thus corresponds to different signal characteristics. For moderate stenosis, there is high-pitched sound at the site of stenosis. In very severe cases, there is no audible sound.
2) The signal feature differs from patient to patient because the angle at AVF junction is different. A slightly change of the angle at AVF junction may cause very different signals in fistula.
3) Stenosis may occur in any position in the fistula. The stenosis position is unknown a priori, so the measurement point should be pre-defined for predictive diagnosis.

In this paper, new signal features being able to overcome the above-mentioned three difficulties are identified and quantified. Additionally, the physiological mechanical explanations of the features are provided. Utilizing the algorithm accompanied with an electronic stethoscope, the diagnosis of AVF stenosis can be performed easily, increasing the possibility for early detection.

II. Methodology

A. Data Acquisition

The AVF signals were measured by 3M Littmann 3200 Electronic Stethoscope with sampling rate of 4000Hz. Each measurement was of 15 seconds and was collected by a trained clinical assistant. 22 patients undergoing PTA treatment participated in this study. Both the signals before and after PTA treatment were collected. Among these patients, three of them underwent PTA treatment twice and one of them

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underwent three times during our data collection period. Totally 54 data sets were collected. This procedure was reviewed and approved by the Research Ethics Committee of National Taiwan University Hospital.

For each data set, five points were measured and collected. The measurement positions were pre-defined and consistent for all patients and can be identified by outward appearance of the fistula. The measurement points were defined as shown in Fig. 1, which were anastomosis (point 1) and 2 cm proximal and distal to the two puncture sites connected to the hemodialysis machine (point 2-5). For the patients with arteriovenous grafts (AVG), the sixth point was measured at the connection of the graft and the vein.

The angiography data during the PTA treatment was collected and examined by the physician. All patients before PTA treatment had over 50% of stenosis, so the pre-PTA data sets were all defined as abnormal cases. For the post-PTA cases, four data sets had residue stenosis more than 50%. These four data sets were considered poor cases and excluded from our study. Other post-PTA measurements had residue stenosis less than 50%, and were considered as normal cases. Totally 50 data sets with normal or abnormal label identified by angiography were used as the gold standard diagnosis result.

B. Feature Extraction

The feature extraction algorithm is developed based on physical examination procedure. The diagnostic characteristics of physical examination are summarized in Table I. from [2].

On the basis of audio signal processing and physical examination, the characteristics for fistula stenosis can be classified to the following four symptoms.

- Symptom 1: Lower energy in normal frequency band or higher energy in ultra-low frequency band
  This symptom occurs when the stenosis is highly severe; namely, the AVF is blocked. There is no audible sound when the AVF is totally blocked and a palpable vibration in ultra-low frequency band may present as the blood flow reflected by the resistance.
- Symptom 2: Systolic only / water-hammer / discontinuity
  If the flow only presents in systolic phase but not in diastolic phase, it implies that the peripheral resistance is higher than normal. This suggests that there is stenosis in the fistula. The discontinuous sound or water-hammer sound is therefore a diagnostic feature for stenosis.
- Symptom 3: High frequency
  Higher frequency implies higher velocity of the blood flow. At the site of stenotic point, the abnormal narrowing of the passageway leads to faster blood flow, hence higher frequency of the signal can be defined as a diagnostic feature.
- Symptom 4: Harmonic sound (seagull murmur)
  Seagull murmur sound is a diagnostic feature for fistula stenosis in physical examination procedure. Although widely consider a high-pitched sound, our research found that seagull murmur is rather a harmonic sound, which may be caused by turbulent flow.

TABLE I. PHYSICAL EXAMINATION

Physical Findings of Venous Stenosis		
Parameters	***Normal***	***Stenosis****
Thrill	Only at the arterial anastomosis	At the site of stenotic lesion
Pulse	Soft, easily compressible	Water hammer
Bruit	Low pitch Continuous Diastolic and systolic	High pitched Discontinuous Systolic only

* Abnormalities listed are for the two extremes: completely normal and severe stenosis. With lesser degrees of stenosis, the changes will be intermediate. Significant stenosis tends to toward the characteristics of a severe lesion.

Each symptom can be quantified by the following features.

- Feature for Symptom 1

The time domain waveforms of signal with symptom 1 and normal AVF signal are shown in Fig. 2. Short-time Fourier transform (STFT) by Hamming window with frequency resolution of 3.9Hz and time resolution of 0.13 second was applied to generate the spectrogram shown in Fig. 3. The resolutions in time and frequency domain are high enough to extract useful time-frequency characteristics of the sound signal. The average energy in each frequency band is calculated, and the extreme values are excluded since noise may present in the measured data. To identify the signal with symptom 1, i.e. lower energy in normal frequency band or higher energy in ultra-low frequency band, the ratio of the energy between the frequency band of less than 50Hz and the frequency band of 100Hz~200Hz is calculated. This is the first feature for the proposed AVF stenosis diagnostic signal processing.

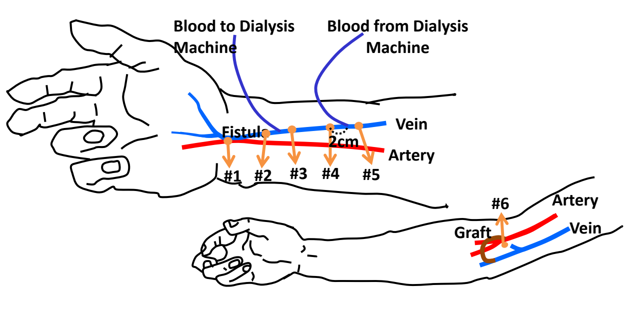

Figure 1. The measurement points.

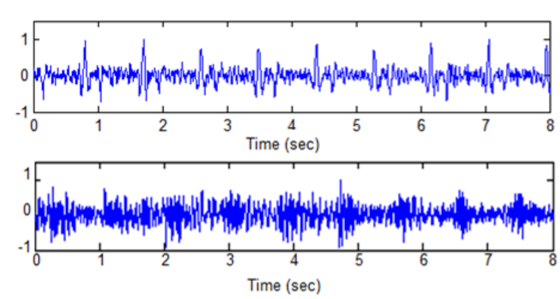

Figure 2. The time domain waveforms of signal with symptom 1 (upper) and normal (lower) AVF signal.

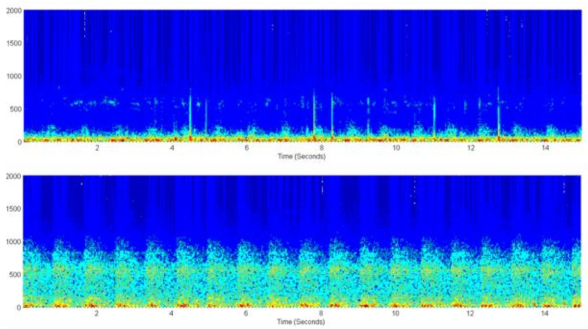

Figure 3. The spectrogram of signal with symptom 1 (upper) and normal (lower) AVF signal. (red: high energy, blue: low energy).

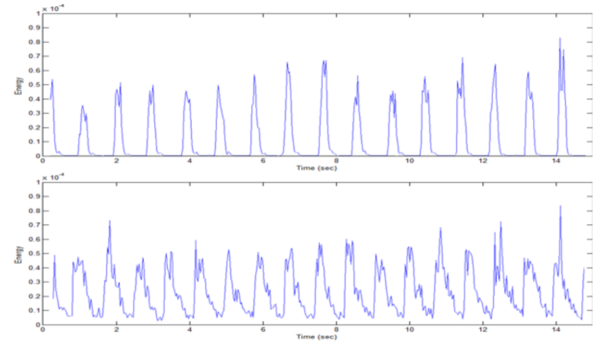

Figure 5. The energy-time plot of signal with water-hammer sound (upper) and normal (lower) AVF signal.

- Features for Symptom 2

The spectrograms of the signal with water-hammer sound and normal AVF signal are shown in Fig. 4. Although one can tell the differences between normal and water-hammer sound by their spectrograms immediately, the diagnostic feature for signal processing is not easy to be quantified from the spectrogram. Thus, energy-time plot is considered. To eliminate the high energy effect in very low frequency band, the measured signal is filtered by an A weighting filter based on 40-phon Fletcher-Munson equal-loudness [11] contour before energy calculation. The A weighting filter simulates human perception to the sound by equalizing the energy in different frequency band. So the energy-time function and the center of frequency function calculated by this method would be close to human perception to the sound. The energy-time plot and the center of frequency plot are shown in Fig. 5 and Fig. 6. For water-hammer sound, the center of frequency differs a lot in systolic and diastolic phase, thus the variation of center of frequency can be defined as a diagnostic feature to specify water-hammer signal from normal signal. Additionally, the variation of the product of center of frequency and energy can extract the abruptness of the emergence of the sound signal, which is another useful feature to diagnose systolic or water-hammer sound.

- Feature for Symptom 3

Using the center of frequency calculated in the above part, the mean of the center of frequency can be another diagnostic feature for AVF stenosis. Based on symptom 3, higher signal frequency may indicate the narrowing of blood flow passageway. If the mean of the center of frequency is abnormally high, it implies that there is a stenosis point near the measurement point.

- Feature for Symptom 4

The seagull murmur can be distinguished easily by human ear, but relatively hard to extract by signal processing. The time-frequency character of seagull murmur sound is shown in Fig. 7. Although seagull murmur sounds like a high-pitched signal, our data shows that it is not in the highest frequency band of the signal. Rather, it is more likely a harmonic sound caused by the resonance of the turbulent flow. However, the flow pattern cannot be seen by angiography, so we do not integrate this feature into our classification system.

In summary, the features of the proposed diagnostic algorithm are as following:

1. The energy ratio between 0-50Hz frequency band and 100-200Hz frequency band. (Symptom 1)
2. Variation of center of frequency. (Symptom 2)
3. Variation of the product of energy and center of frequency. (Symptom 2)
4. Mean of center of frequency. (Symptom 3)

C. Classification

The aforementioned four features are calculated from each measured signal for all time and rescaled by an exponential function, optimizing the weighting of each feature. The features in the same data set are combined together. Then, a subset of the features is chosen and fed into the classifier. Support vector machine (SVM) with Gaussian radial basis kernel function (RBF) is used for classification in our system [12]-[15]. Two-fold cross-validation is performed for 100

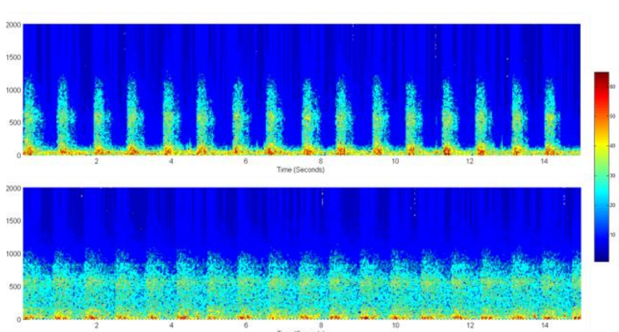

Figure 4. The spectrogram of signal with water-hammer sound (upper) and normal (lower) AVF signal. (red: high energy, blue: low energy)

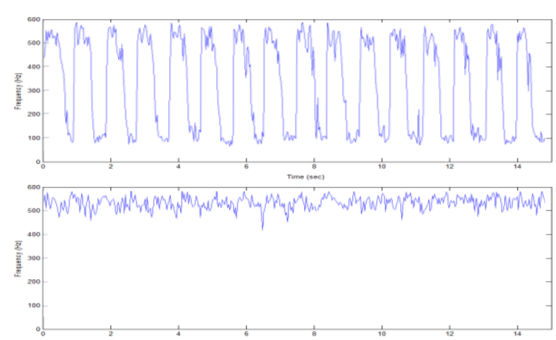

Figure 6. The center of frequency of signal with water-hammer sound (upper) and normal (lower) AVF signal.

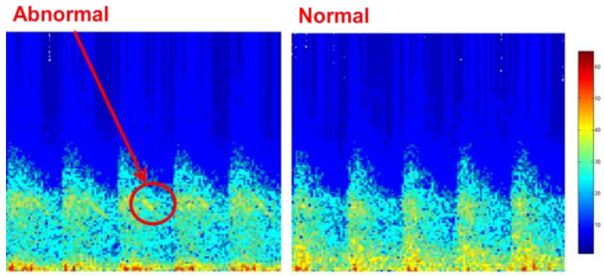

Figure 7. The harmonic sound/ seagull murmur/ turbulent flow in spectrogram.

times, that is, choosing half data sets randomly to develop the classifier and use the other half data sets to test the average hit-rate of the classifier for 100 times. There is no overlap between the test sets and the training sets. This procedure is implemented to prevent model over-fitting.

III. Results and Discussion

Our research result shows that the measured signals at point 1 (AV junction), point 5, and point 6 for AVG are not discriminative for AVF stenosis. For point 1, the possible explanation is that the signal in AV junction depends largely on the angle between the artery and vein. Thus, the signal feature differs from patient to patient, and cannot be a general feature for stenosis diagnosis among all kinds of patients. As for point 5 and 6, the flow is generally too weak to be discerned.

Signal at point 4 is the most discriminative for AVF stenosis detection. Choosing the features of point 4 as the subset fed into our classifier, an average two-fold cross-validation hit-rate of 84.3% can be obtained. This means that the system correctly tell 84.3% of the test signals whether they belong to the pre-PTA group (stenosis > 50%) or the post-PTA group (stenosis < 50%). Additionally, adding features of other points to the sub set fed into the classifier can improve the average hit-rate up to more than 90%. The sensitivity is 86.2% and the specificity is 95.2%; and the positive predictive value is 96.2% and negative predictive value is 83.3%. This result shows that this algorithm is an excellent computer-aided diagnostic tool for AVF stenosis detection.

Back to the three feature extraction difficulties mentioned in section I. The first difficulty is eliminated by our multi-feature classification algorithm. The second difficulty can be solved by choosing point 4 as measurement point, which depends less on AVF geometry. Finally, for the third difficulty, no matter stenosis occurs at any position of the fistula, one of our proposed signal features of point 4 would change accordingly. Therefore, our proposed system can be used for AVF stenosis diagnosis in a very general situation.

IV. Conclusion

In this paper, a physiology-based computer-aided diagnostic algorithm for AVF stenosis detection is developed with satisfying performance. The advantage of our system is that the classification model is based on large data set with cross-validation and is highly consistent with angiography. Also, the diagnostic features follow from physical examination, which has physiological meaning and mechanistic explanation. This diagnosis algorithm provides a useful tool for early detection of AVF stenosis for ESRD patients.

V. Acknowledgment

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